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Review Article

Nutraceuticals for Molecular level Obesity Management; A Review of Its Possible Role on Obesity's Metabolic Consequences and Obesity Management

Mohammad Nadeem Khan[1]* and Praveen Chandra Dubey[2]

[1]*Department of Pharmacology, Clinical Pharmacology, Sri Aurobindo Medical College and PG Institute, Sri Aurobindo University, Indore, Madhya Pradesh, India*

[2]*Chairman SEAC, Government of Madhya Pradesh Bhopal Madhya Pradesh, India*

***Corresponding Author:** Mohammad Nadeem Khan, Department of Pharmacology, Clinical Pharmacology, Sri Aurobindo Medical College and PG Institute, Sri Aurobindo University, Indore, Madhya Pradesh, India.

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Abstract

The rising global prevalence of obesity has led to increased research interest in novel strategies for its management. This review explores the potential role of nutraceuticals in mitigating obesity's metabolic consequences at the molecular level. Nutraceuticals, bioactive compounds derived from food, have shown promise in modulating various pathways associated with obesity, including inflammation, lipid metabolism, and insulin sensitivity. The metabolic consequences of obesity encompass a spectrum of disturbances, including insulin resistance, chronic inflammation, dyslipidemia, and oxidative stress. Nutraceuticals offer a unique approach by targeting these pathways at the molecular level. For instance, green tea extract containing epigallocatechin gallate (EGCG) has demonstrated potential in enhancing fat oxidation and metabolic rate. Omega-3 fatty acids from fish oil exhibit anti-inflammatory effects, addressing one of the key metabolic consequences of obesity. Formulating stable and high-quality supplements is paramount to ensuring consistent efficacy. Moreover, a personalized approach considering individual variations in response to nutraceuticals may enhance outcomes. Identifying specific strains of probiotics with proven efficacy in modulating gut microbiota, a key player in metabolic health, is crucial. Additionally, combinations of nutraceuticals that target multiple pathways simultaneously may have synergistic effects, providing a comprehensive approach to reducing the metabolic consequences of obesity. It is essential to emphasize that nutraceuticals should be viewed as complementary to lifestyle interventions, including a balanced diet and regular physical activity. Further research and clinical studies are warranted to validate the efficacy and safety of nutraceutical interventions, paving the way for more targeted and personalized approaches to obesity management.

Keywords: Functional Foods; Bioactive Compounds; Weight Management; Obesity; Metabolic Consequences; Thermogenesis; Appetite Regulation; Fat Metabolism; Blood Glucose; Inflammation; Gut Microbiota; Antioxidants; Hormonal Regulation

Introduction

The escalating global obesity epidemic has become a formidable public health challenge, demanding creative and effective strategies for prevention and management. The global prevalence of obesity has reached epidemic proportions, posing significant challenges to public health worldwide [1]. Amidst the array of interventions under consideration, functional foods, distinguished by their enrichment with bioactive compounds, have emerged as a focal point of interest. Various factors such as increased food consumption, sedentary lifestyles, positive energy balance, and the emergence of food addiction contribute to the escalating rates of obesity and its associated chronic diseases [2]. In response, there has been a growing interest in exploring the potential health benefits of bioactive compounds present in certain foods, often referred to as functional foods [3]. These compounds, including resveratrol, epigallocatechin, curcumin, quercetin, ellagic acid, anthocyanins, b-glucans, and others, have been investigated for their direct or indirect effects on molecular pathways associated with cardiovascular diseases, diabetes, metabolic syndrome, and cancer [4]. Epidemiological data have consistently supported the association between a high intake of natural functional foods and a decreased risk of chronic diseases, including cardiovascular diseases, cancer,

metabolic syndrome, type II diabetes, and obesity [5]. The urgency of addressing this epidemic necessitates a departure from conventional approaches towards innovative and holistic solutions. Nutraceuticals represent a paradigm shift in the field of nutrition, extending beyond their conventional role in providing basic nutrients. Enriched with bioactive compounds, these foods offer the potential to exert specific physiological effects, positioning them as promising candidates for combating the intricate web of metabolic dysregulation associated with obesity [6]. The appeal of Nutraceuticals lies in their ability to influence various aspects of metabolism. From thermogenic properties that enhance energy expenditure to appetite regulation mechanisms that curb overconsumption, these foods present a holistic approach to address the multifaceted challenges posed by obesity [7]. Various Nutraceuticals compounds, such as resveratrol, epigallocatechin-3-gallate (EGCG), curcumin, quercetin, ellagic acid, and anthocyanins, are found in specific food sources. For example, resveratrol is present in grapes, red wine, and pomegranates, while EGCG is abundant in green tea [8]. These compounds are characterized by their antioxidant, anti-inflammatory, and chemo-preventive properties. Obesity, characterized by an excess accumulation of body fat, has become a global epidemic with implications for various chronic degenerative and inflammatory diseases [9]. Factors contributing to obesity include increased food consumption, decreased physical activity, positive energy balance, and the emergence of food addiction. Efforts to address obesity and its metabolic consequences have led to a focus on weight control strategies, including increased energy expenditure and adherence to a balanced diet. Recent research emphasizes the potential role of functional foods, such as gojiberry, cranberry, and pomegranate, in weight management [10]. Clinical studies with 300 healthy volunteers demonstrated a decreased Body Mass Index (BMI) in those regularly consuming these functional foods. Scientific evidence suggests that specific bioactive compounds and functional foods, including b-glucans, glucomannan, and foods with reduced fat and sugar content, may contribute to weight management and mitigate metabolic consequences in obese individuals [11]. However, it is crucial to highlight that these benefits are contingent on the incorporation of these functional foods into a balanced diet and not through unilateral and excessive consumption. By elevating metabolic rates, these compounds contribute to calorie expenditure, offering a potential avenue for weight management. Functional foods, particularly those rich in dietary fiber, play a pivotal role in appetite regulation [11]. By promoting a sense of fullness and satiety, they act as allies in curbing excessive caloric intake, a critical aspect of effective weight management. Functional foods are not solely focused on weight loss but extend their influence to mitigate the metabolic consequences associated with obesity [12]. This includes interventions in blood glucose regulation, inflammation modulation, gut microbiota balance, and antioxidant effects. The incorporation of functional foods enriched with bioactive compounds represents a promising and innovative strategy in the battle against global obesity. As these foods influence various facets of metabolism, they offer a comprehensive approach that extends beyond mere weight loss. Further research and exploration of the nuanced interactions between functional foods and metabolic pathways are imperative for optimizing their effectiveness and establishing evidence-based dietary guidelines for population-wide obesity prevention and management [13]. This review critically examines recent studies exploring the potential roles and effects of specific Nutraceutics compounds and functional foods in weight management and the metabolic consequences of obesity. While promising findings suggest the positive impact of these compounds, further research, including clinical and epidemiological studies, is essential to validate and ensure their efficacy.

Metabolic consequences

Obesity's metabolic consequences refer to the various physiological and biochemical changes that occur in the body as a result of excessive accumulation of body fat [14]. These consequences can have profound effects on overall health and are associated with an increased risk of several chronic conditions. Certainly, the metabolic consequences of obesity are diverse and impact various physiological systems in the body. Addressing obesity and its metabolic consequences typically involves lifestyle interventions, including dietary changes, increased physical activity, and, in some cases, medical or surgical interventions [15]. Early intervention is crucial to preventing or mitigating the long-term metabolic complications associated with obesity.

Insulin resistance

Obesity is a major contributor to insulin resistance, and the excess accumulation of fat, especially visceral fat, plays a crucial role in its development. In summary, the interplay between insulin resistance and impaired pancreatic function in the context of obesity creates an environment conducive to the development of type 2 diabetes. Obesity plays a pivotal role in the pathophysiology of insulin resistance, contributing significantly to the development and progression of this metabolic condition [16]. The relationship between obesity and insulin resistance involves complex interactions at the molecular, cellular, and systemic levels [17]. Obesity is characterized by an excessive accumulation of adipose tissue, especially visceral fat. Enlarged adipocytes in obesity release pro-in-

flammatory cytokines, leading to chronic low-grade inflammation. Dysfunctional adipose tissue secretes adipokines, such as leptin and resistin, which can contribute to insulin resistance. In obesity, increased lipolysis results in elevated levels of circulating FFAs [18]. High levels of FFAs can impair insulin signaling in various tissues, contributing to insulin resistance. Macrophage Infiltration: In obese adipose tissue, there is an infiltration of immune cells, particularly macrophages. Macrophages release inflammatory cytokines (e.g., TNF-α, IL-6), which interfere with insulin signaling pathways. Prolonged exposure to elevated insulin levels, as seen in obesity, can lead to downregulation of insulin receptors. Inflammatory signaling and excess FFAs can impair the activation of IRS, a critical mediator in insulin signaling [19]. Excess FFAs can accumulate in non-adipose tissues (lipotoxicity), contributing to mitochondrial dysfunction. Impaired Mitochondrial dysfunction leads to impaired oxidative phosphorylation and increased production of reactive oxygen species (ROS), further disrupting insulin signaling [20]. Lipid overload and inflammation in obesity contribute to endoplasmic reticulum (ER) stress. ER stress activates the UPR, which can interfere with insulin signaling pathways. Insulin resistance affects various downstream signaling events, including impaired glucose uptake in muscle cells and reduced suppression of hepatic glucose production. Glucose Transporter Dysfunction: Reduced translocation of glucose transporters (e.g., GLUT4) to the cell membrane hinders glucose uptake. Initially, the pancreas compensates for insulin resistance by increasing insulin production [21]. Prolonged exposure to high insulin levels can lead to beta-cell exhaustion and impaired insulin secretion. As insulin resistance progresses, the inability of tissues to respond to insulin leads to elevated blood glucose levels. Insulin resistance contributes to dyslipidemia, with increased triglycerides and reduced HDL cholesterol. Understanding the intricate links between obesity and insulin resistance is crucial for developing effective strategies for prevention and management [22].

Dyslipidemia

Dyslipidemia refers to an abnormality in lipid (fat) levels in the bloodstream, and it is a common metabolic consequence of obesity. The lipid profile typically includes measurements of triglycerides, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) [23]. The metabolic pathophysiology of dyslipidemia in obesity involves a complex interplay of various factors, including adipose tissue dysfunction, inflammation, insulin resistance, and altered lipid metabolism. Increased Obesity is characterized by an excess accumulation of adipose tissue, especially visceral fat. Enlarged adipocytes in obesity release pro-inflammatory adipokines and cytokines, contributing to systemic inflammation [24]. Dysfunctional adipose tissue influences lipid metabolism, leading to increased release of free fatty acids (FFAs) into the bloodstream. In obesity, there is increased lipolysis in adipose tissue, releasing FFAs [25]. Elevated FFAs contribute to increased synthesis of triglycerides in the liver. Insulin resistance leads to an imbalance in lipid metabolism, contributing to increased triglyceride synthesis in the liver and decreased clearance of triglyceride-rich lipoproteins [26]. Insulin resistance and elevated FFAs stimulate the liver to produce more very-low-density lipoproteins (VLDLs), which are rich in triglycerides. Insulin resistance is associated with reduced production and increased clearance of high-density lipoprotein cholesterol (HDL-C), contributing to low HDL-C levels. Inflammatory Cytokines: Chronic low-grade inflammation in obesity, characterized by elevated levels of cytokines like TNF-α and IL-6, contributes to dyslipidemia [27]. Inflammation can disrupt normal lipid metabolism, influencing the synthesis and clearance of lipoproteins. Obesity-induced lipid overload and inflammation can lead to endoplasmic reticulum (ER) stress in hepatocytes.ER stress may impair lipid metabolism and contribute to dyslipidemia [28]. Enlarged and dysfunctional adipocytes in obesity may have reduced capacity to store excess lipids. Reduced lipid storage capacity in adipose tissue can lead to increased circulating levels of triglycerides. Certain genetic factors may contribute to both obesity and dyslipidemia [29]. Genetic variants can influence lipid metabolism and contribute to dyslipidemia in the context of obesity. Understanding these metabolic pathways helps to comprehend how obesity contributes to dyslipidemia. The imbalance in lipid metabolism, characterized by increased synthesis and reduced clearance of triglycerides, elevated LDL-C, and decreased HDL-C, collectively contributes to the dyslipidemic profile associated with obesity [30].

Non-alcoholic fatty liver disease (NAFLD)

NAFLD is characterized by the excessive accumulation of fat in the liver, not due to excessive alcohol consumption [31]. NAFLD encompasses a spectrum of conditions, ranging from simple steatosis (fat accumulation) to more severe forms like non-alcoholic steatohepatitis (NASH) and cirrhosis. In the early stages, the primary effect is the accumulation of triglycerides in hepatocytes, leading to simple steatosis, which may be asymptomatic [32]. NASH involves not only fat accumulation but also inflammation and liver cell damage. It is a more progressive and potentially serious form of NAFLD. In advanced stages, prolonged inflammation and liver cell damage can lead to the development of fibrosis and cirrhosis, characterized by extensive scarring and loss of normal liver function. Persistent

inflammation in NASH can lead to fibrosis, where scar tissue replaces normal liver tissue [33]. Fibrosis and cirrhosis can impair liver function, affecting its ability to detoxify the blood, produce proteins, and regulate various metabolic processes. Advanced stages of NAFLD, especially cirrhosis, increase the risk of complications such as liver failure, hepatocellular carcinoma (liver cancer), and portal hypertension. Insulin resistance, often present in obesity, is closely associated with the development of NAFLD. Insulin resistance contributes to increased lipolysis, leading to elevated levels of free fatty acids in the liver, promoting fat accumulation. In obesity, the chronic low-grade inflammation associated with adipose tissue dysfunction can extend to the liver, contributing to the inflammatory component of NAFLD [34]. Increased oxidative stress in the liver, resulting from a disrupted balance between reactive oxygen species (ROS) and antioxidants, plays a role in the progression of NAFLD. The molecular pathophysiology of Non-Alcoholic Fatty Liver Disease (NAFLD) in obesity involves intricate interactions among various cellular and molecular processes. In obesity, increased delivery of free fatty acids to the liver, often due to insulin resistance, leads to enhanced triglyceride synthesis and storage in hepatocytes. Dysfunctional adipose tissue contributes to elevated circulating free fatty acids, exacerbating lipid accumulation in the liver. Impaired insulin signaling in the liver is a hallmark of insulin resistance. This leads to increased gluconeogenesis and lipogenesis, contributing to elevated hepatic fat content. Insulin resistance in adipose tissue results in increased lipolysis, releasing more free fatty acids into the bloodstream and further contributing to hepatic lipid accumulation [35]. Activation of Inflammatory Cascades: Inflammatory cytokines, such as TNF-α and IL-6, activate signaling pathways (e.g., JNK, NF-κB) that promote inflammation and may contribute to hepatocellular injury. Elevated lipid accumulation and inflammation contribute to increased oxidative stress in hepatocytes. Oxidative stress can impair mitochondrial function, further contributing to lipid accumulation and hepatocyte injury. Impaired Beta-Oxidation: Mitochondrial dysfunction in NAFLD may result in reduced beta-oxidation of fatty acids. Impaired mitochondrial function can lead to the accumulation of lipid intermediates, contributing to cellular stress [36]. The excess lipid load in hepatocytes can induce ER stress.ER stress triggers the UPR, attempting to restore cellular homeostasis, but prolonged ER stress can contribute to hepatocyte injury. In response to injury and inflammation, hepatic stellate cells may become activated. Activated stellate cells produce excessive extracellular matrix, leading to fibrosis and scarring of the liver. Certain genetic factors may influence an individual's susceptibility to developing NAFLD. Epigenetic changes, such as DNA methylation and histone modifications, may play a role in the regulation of genes involved in lipid metabolism and inflammation [37]. Understanding these molecular pathways provides insight into the complexity of NAFLD development in the context of obesity. Therapeutic approaches targeting these molecular processes, such as medications addressing insulin resistance, anti-inflammatory agents, and antioxidants, are areas of active research. Lifestyle interventions, including weight loss, a balanced diet, and increased physical activity, remain central to the management of NAFLD by addressing both the molecular and systemic aspects of the condition. Early detection and intervention are crucial to prevent the progression of NAFLD to more severe stages [38].

Cardiovascular diseases in obesity

Chronic inflammation associated with obesity contributes to endothelial dysfunction. Inflammatory cytokines and adipokines released by adipose tissue can impair the function of the endothelium, the inner lining of blood vessels. Endothelial dysfunction is a key step in the initiation of atherosclerosis, promoting the adhesion of immune cells and the formation of atherosclerotic plaques. Atherosclerosis is the buildup of plaques containing cholesterol, lipids, and inflammatory cells in arterial walls [39]. Dyslipidemia associated with obesity contributes to the deposition of cholesterol in blood vessel walls. Atherosclerosis narrows and stiffens arteries, reducing blood flow and increasing the risk of cardiovascular events. Obesity is strongly linked to the development of hypertension. Increased adiposity leads to the release of factors that raise blood pressure, such as angiotensin-II and aldosterone. Hypertension places additional stress on the heart and blood vessels, contributing to cardiovascular diseases [40]. Insulin resistance, common in obesity, is associated with hyperinsulinemia (elevated insulin levels). Hyperinsulinemia may promote the growth of smooth muscle cells in blood vessel walls and enhance sodium retention, contributing to hypertension. Insulin resistance and hyperinsulinemia are implicated in the development of atherosclerosis and hypertension. Excess circulating lipids can infiltrate and accumulate in non-adipose tissues, leading to lipotoxicity. Lipotoxicity contributes to inflammation, oxidative stress, and damage to blood vessels, promoting atherosclerosis. Obesity is associated with increased oxidative stress. Oxidative stress damages cells, including those in blood vessel walls, promoting inflammation and atherosclerosis. Oxidative stress contributes to the progression of cardiovascular diseases. Adipose tissue secretes adipokines, including pro-inflammatory cytokines [41]. Elevated levels of inflammatory mediators contribute to systemic inflammation. Chronic inflammation is a key driver of cardiovascular diseases, promoting plaque

formation and destabilization. Distribution of fat in the visceral (abdominal) area is common in obesity. Visceral fat is metabolically active and releases substances that contribute to insulin resistance, inflammation, and cardiovascular risk. Increased visceral fat is associated with a higher risk of cardiovascular diseases. Obesity can activate the RAAS, a system that regulates blood pressure and fluid balance. RAAS activation contributes to vasoconstriction, sodium retention, and increased blood pressure [42]. Persistent activation of RAAS is linked to hypertension and cardiovascular diseases. Molecular pathophysiology of cardiovascular diseases in obesity involves recognizing the intricate interactions among inflammation, metabolic dysfunction, oxidative stress, and hormonal regulation [43].

Reproductive issues in obesity

Obesity can have significant effects on the reproductive system in both men and women. The impact of obesity on reproductive health is multifaceted and involves various hormonal, metabolic, and structural changes. Obesity disrupts the balance of hormones involved in reproductive function. In females, excess adipose tissue can lead to increased production of estrogen from adipocytes, disrupting the normal hormonal balance [44]. In males, obesity is associated with decreased levels of testosterone and increased conversion of testosterone to estrogen in adipose tissue. Hormonal imbalance can impact the menstrual cycle in women and reduce sperm quality in men [45]. Other obesity related consequence men and women summarized in table 1. The molecular pathways involved in reproductive issues associated with obesity is crucial for developing targeted interventions.

Description	Women	Men
Hormonal Imbalance	Estrogen Overproduction: Adipose tissue can produce estrogen, leading to hormonal imbalances. Insulin Resistance: Obesity is associated with insulin resistance, impacting ovarian function and hormone regulation.	Reduced Testosterone: Obesity is associated with lower testosterone levels in men. Increased Estrogen Conversion: Adipose tissue can convert testosterone to estrogen, altering hormonal balance.
Inflammation and Oxidative Stress	Ovarian Inflammation: Chronic inflammation in obesity may affect the ovaries, impacting follicular development. Oxidative Stress: Increased oxidative stress can influence oocyte quality.	Sperm Quality: Increased oxidative stress in obesity can affect sperm quality and DNA integrity. Testicular Inflammation: Chronic inflammation may impact testicular function and spermatogenesis.
Leptin and Adiponectin Dysregulation	Leptin Resistance: Elevated levels of leptin, a hormone produced by adipose tissue, can lead to leptin resistance and disrupt ovarian function. Reduced Adiponectin: Lower levels of adiponectin, another adipokine, may impact insulin sensitivity and ovarian function.	Leptin Receptor Expression: Altered expression of leptin receptors in the testes may affect spermatogenesis. Adiponectin Influence: Adiponectin may play a role in Leydig cell function and testosterone production.
Impact on Ovulation and Fertility	Ovulatory Dysfunction: Obesity is associated with impaired ovulation, contributing to fertility issues. Reduced Fertility: Obesity is linked to a longer time to conceive and reduced overall fertility.	Impaired Sperm Quality: Obesity is associated with reduced sperm count, motility, and morphology. Lower Fertility Rates: Increased time to conceive and lower overall fertility.
Pregnancy Complications:	Gestational Diabetes: Increased risk of gestational diabetes during pregnancy. Hypertension and Preeclampsia: Higher incidence of hypertension and preeclampsia.	
Impact on Sexual Function:		Erectile Dysfunction: Obesity is a risk factor for erectile dysfunction, affecting sexual function. Reduced Libido: Changes in hormonal balance and overall health may impact sexual desire.

Table 1: Simplified table summarizing the molecular-level effects of obesity on the reproductive system in both men and women.

Joint Problems in obesity

The molecular pathophysiology of joint problems associated with excess weight, particularly in the context of osteoarthritis, involves various mechanisms at the cellular and molecular levels. Osteoarthritis is a degenerative joint disease characterized by the breakdown of cartilage in the joints, leading to joint pain and reduced mobility [46]. Excess adipose tissue (fat) is known to produce pro-inflammatory molecules called cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha). Systemic inflammation contributes to the activation of inflammatory pathways in joint tissues. Adipose tissue secretes adipokines, including adiponectin and leptin, which can influence cartilage metabolism and contribute to the inflammatory environment in joints [47]. Leptin, in particular, has been associated with the promotion of inflammation and cartilage degradation in osteoarthritis. Increased mechanical load and inflammation in joints can upregulate the expression of MMPs, enzymes that play a role in breaking down the extracellular matrix of cartilage. MMPs contribute to the degradation of collagen and proteoglycans in the cartilage, leading to loss of structural integrity. Reactive oxygen species (ROS) can damage cells and exacerbate the breakdown of cartilage [48]. Obesity is often associated with insulin resistance and metabolic dysfunction. Insulin resistance may contribute to the activation of inflammatory pathways and alter the balance of factors regulating cartilage homeostasis. Increased body weight places additional mechanical stress on weight-bearing joints. This excessive mechanical load contributes to wear and tear on the joint surfaces, accelerating the degenerative processes in the cartilage [49]. The synovium, a membrane surrounding joints, can become inflamed due to systemic factors and increased mechanical stress. Inflammation of the synovium further contributes to joint pain and dysfunction [50].

Cancer in obesity

The molecular pathophysiology linking obesity to an increased risk of certain cancers involves complex interactions between adipose tissue, inflammation, hormonal imbalances, and alterations in cellular signaling pathways. Adipose tissue, particularly visceral fat, produces pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha). Chronic low-grade inflammation in obesity creates a favorable microenvironment for cancer development and progression [51]. Adipokines, such as leptin and adiponectin, play a role in regulating energy balance and inflammation. Dysregulation of these adipokines in obesity can contribute to insulin resistance, chronic inflammation, and the promotion of cancer cell survival and proliferation [52]. Obesity is linked to alterations in sex hormones, particularly increased estrogen levels. Elevated estrogen levels, as seen in postmenopausal women with obesity, are associated with an increased risk of breast and endometrial cancers [53]. Persistent high blood glucose levels in obesity can contribute to cancer development and progression. Hyperglycemia may fuel the growth of cancer cells through increased availability of glucose, a crucial energy source. Adipose tissue secretes various bioactive molecules, including fatty acids and adipokines, which can directly influence cancer cell behavior. Free fatty acids, for example, may promote inflammation and cancer cell survival. The mammalian target of rapamycin (mTOR) pathway, involved in cell growth and proliferation, is often dysregulated in obesity. Dysregulation of mTOR signaling can contribute to uncontrolled cell growth and survival in cancer. Obesity can impact the composition of the gut microbiota, leading to changes in microbial metabolites and inflammation. Disruptions in gut microbiota have been linked to an increased risk of colorectal cancer [54].

Nutraceuticals uses in obesity management

Nutraceuticals, which include bioactive compounds found in food or extracted for use as supplements, have been the subject of various molecular studies to understand their potential roles in addressing obesity and its metabolic consequences [55]. Table 2 given some examples of nutraceuticals and the molecular studies that have explored their effects on obesity management. It's important to note that while these molecular studies provide insights into the potential mechanisms of action, the translation to clinical outcomes may vary, and more research is often needed. Additionally, individual responses can differ, and the overall impact of nutraceuticals on obesity and metabolic consequences should be considered in the context of a holistic approach to health, including lifestyle modifications and a balanced diet [56]. Always consult with a healthcare professional before incorporating new supplements into your routine, especially for managing obesity and related conditions. Several nutraceuticals have been studied for their potential role in reducing insulin resistance, a condition where the body's cells become less responsive to the effects of insulin. Reducing insulin resistance is important for managing conditions like type 2 diabetes and metabolic syndrome [57]. There are some nutraceuticals that have been investigated for their impact on insulin resistance that is summarized in table 3.

It's important to note that while these nutraceuticals show promise in research studies, individual responses can vary, and

Nutraceutics	Molecular Studies	Implications:
Green Tea Extract (Epigallocatechin Gallate - EGCG):	Molecular Studies: EGCG in green tea has been studied for its effects on adipocyte differentiation, lipid metabolism, and thermogenesis. Molecular mechanisms include modulation of AMP-activated protein kinase (AMPK), peroxisome proliferator-activated receptor gamma (PPARγ), and uncoupling protein (UCP) expression	Green tea extract may influence adipose tissue metabolism and thermogenic processes, potentially contributing to weight management.
Berberine	Berberine has been investigated for its impact on AMPK activation, insulin signaling pathways, and inflammation. It may also affect gene expression related to glucose and lipid metabolism.	Berberine's molecular effects suggest potential benefits in improving insulin sensitivity and metabolic parameters, making it relevant for obesity and related conditions
Curcumin (Turmeric Extract)	Curcumin has been studied for its anti-inflammatory effects, modulation of adipokine expression, and influence on insulin signaling pathways, including inhibition of nuclear factor-kappa B (NF-κB).	The molecular actions of curcumin suggest its potential in mitigating inflammation and improving insulin sensitivity, which can be relevant for managing obesity-related metabolic consequences
Resveratrol	Resveratrol, found in red grapes and wine, has been investigated for its effects on sirtuin activation, AMPK activation, and modulation of genes involved in lipid metabolism and inflammation.	Molecular studies suggest that resveratrol may have metabolic benefits, potentially influencing weight management and improving insulin sensitivity
Omega-3 Fatty Acids	Omega-3 fatty acids, especially EPA and DHA, have been studied for their anti-inflammatory effects, influence on adipokine expression, and modulation of lipid metabolism genes	Molecular studies indicate that omega-3 fatty acids may contribute to reducing inflammation and improving lipid metabolism, supporting weight management.
Quercetin	Quercetin has been investigated for its antioxidant and anti-inflammatory effects, including modulation of NF-κB and peroxisome proliferator-activated receptor alpha (PPARα) pathways.	Molecular studies suggest that quercetin may have potential in mitigating inflammation and improving lipid metabolism, which could impact obesity-related metabolic consequences.
Capsaicin	Capsaicin, found in chili peppers, has been studied for its effects on thermogenesis, activation of transient receptor potential channels, and modulation of genes related to energy expenditure	Molecular studies suggest that capsaicin may influence metabolic processes, potentially aiding in weight management

Table 2: Some examples of nutraceuticals and the molecular studies that have explored their effects on obesity management.

Nutraceutics	Mode of action	Implications:
Cinnamon	Cinnamon has been studied for its ability to improve insulin sensitivity by enhancing insulin signaling and glucose uptake in cells	Effects on Insulin Resistance: Some studies suggest that cinnamon supplementation may help improve insulin sensitivity in individuals with insulin resistance
Berberine	Berberine, a compound found in several plants, may activate AMP-activated protein kinase (AMPK), a cellular energy sensor, leading to improved glucose metabolism	Effects on Insulin Resistance: Berberine has shown promise in improving insulin sensitivity and reducing insulin resistance in various studies
Alpha-Lipoic Acid	Alpha-lipoic acid is an antioxidant that may enhance insulin sensitivity by improving glucose uptake and reducing oxidative stress	Effects on Insulin Resistance: Studies have suggested that alpha-lipoic acid supplementation may benefit individuals with insulin resistance, particularly in conditions like type 2 diabetes
Curcumin (Turmeric Extract)	Curcumin, the active compound in turmeric, has anti-inflammatory and antioxidant properties that may influence insulin signaling pathways	Effects on Insulin Resistance: Some studies propose that curcumin supplementation may improve insulin sensitivity and reduce markers of inflammation in insulin-resistant individuals

Omega-3 Fatty Acids	Omega-3 fatty acids, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), may have anti-inflammatory effects and improve insulin sensitivity	Effects on Insulin Resistance: Fish oil supplementation, rich in omega-3 fatty acids, has been associated with improved insulin sensitivity in various studies
Magnesium	Magnesium is involved in insulin action and glucose metabolism. It plays a role in cellular glucose uptake and insulin receptor activity	Effects on Insulin Resistance: Magnesium supplementation may help improve insulin sensitivity, and magnesium deficiency has been linked to insulin resistance
Vitamin D	Vitamin D is involved in insulin secretion and insulin sensitivity. It may also have anti-inflammatory effects	Effects on Insulin Resistance: Some research suggests that maintaining adequate vitamin D levels may contribute to better insulin sensitivity
Quercetin	Quercetin, a flavonoid found in various fruits and vegetables, has antioxidant and anti-inflammatory properties that may impact insulin sensitivity	Effects on Insulin Resistance: Studies have explored the potential of quercetin supplementation in improving insulin sensitivity and reducing inflammation

Table 3: Some nutraceuticals that have been investigated for their impact on insulin resistance.

their efficacy may depend on factors such as dosage, duration, and the specific population studied [58]. Always consult with a healthcare professional before incorporating new supplements into your routine, especially if you have existing health conditions or are taking medications. Nutraceuticals should complement a comprehensive approach to managing insulin resistance, including a balanced diet, regular exercise, and lifestyle modifications. Nutraceuticals, which are food or food products that provide health benefits in addition to their basic nutritional value, can play a role in supporting obesity reduction when incorporated into a comprehensive approach that includes a healthy diet, regular physical activity, and lifestyle modifications [59]. It's crucial to approach the use of nutraceuticals for obesity reduction with caution. Consult with a healthcare professional before incorporating new supplements into your routine, as individual responses can vary, and some products may interact with medications or have potential side effects [60]. Table-4 concluded some nutraceuticals that have significant role in obesity reduction.

Several nutraceuticals have been studied for their potential role in weight loss. It's important to note that individual responses to these supplements can vary, and their effectiveness may depend on factors such as diet, exercise, and overall health [61]. Always consult with a healthcare professional before incorporating any new supplements into your routine. It's crucial to approach weight loss with a holistic perspective that includes a balanced diet, regular physical activity, and healthy lifestyle habits. The molecular modes of action of nutraceuticals in weight loss or their role in addressing obesity's metabolic consequences can vary depending on the specific compound [62]. It's important to note that while these mechanisms have been studied to varying degrees, the evidence supporting the efficacy of some nutraceuticals in weight loss is not always robust.

Nutraceutics	Description
Green Tea Extract	EGCG in green tea has been studied for its potential to increase thermogenesis and fat oxidation. It may also have anti-inflammatory effects and influence lipid metabolism. Green tea contains compounds such as catechins and caffeine, which may boost metabolism and aid in fat oxidation. Some studies suggest that green tea extract can contribute to weight loss and fat loss.
Conjugated Linoleic Acid (CLA)	CLA may influence enzymes involved in fat metabolism and adipocyte (fat cell) function. It is suggested to modulate lipid metabolism and reduce fat storage. CLA is a type of fatty acid found in meat and dairy products or available as a supplement. Research has indicated potential benefits for weight management and fat loss, although results can vary
Probiotics	Probiotics can modulate the gut microbiota, influencing metabolic processes and inflammation. They may also affect energy balance and nutrient absorption By promoting satiety, glucomannan may help control appetite and support weight loss efforts. The gut microbiota has been linked to obesity, and certain probiotics may influence the composition of gut bacteria in a way that supports weight management. Yogurt, kefir, and dietary supplements are common sources of probiotics
Fiber	Soluble fiber, found in foods like oats, beans, and fruits, may contribute to satiety and weight management. Some nutraceuticals also provide concentrated forms of fiber,

Omega-3 Fatty Acids	Found in fatty fish, flaxseeds, and walnuts, omega-3 fatty acids may have anti-inflammatory effects and could potentially contribute to weight loss when combined with a calorie-controlled diet
Chromium	Chromium is involved in insulin signaling and glucose metabolism. It may enhance insulin sensitivity and regulate blood sugar levels. Chromium is a mineral that plays a role in insulin function and glucose metabolism. Some studies suggest that chromium supplementation may help with weight loss, although results are mixed
Garcinia Cambogia	HCA, the active ingredient in *Garcinia cambogia*, is believed to inhibit an enzyme called citrate lyase, which is involved in the synthesis of fatty acids. This tropical fruit extract has been studied for its potential to inhibit fat production and suppress appetite. However, more research is needed to establish its efficacy and safety
Caffeine	Caffeine is a natural stimulant found in coffee, tea, and some weight loss supplements. It may increase metabolism and enhance fat burning
Glucomannan	Glucomannan is a soluble fiber that absorbs water, forming a gel-like substance. This may contribute to feelings of fullness and reduce calorie intake. Derived from the root of the konjac plant, glucomannan is a soluble fiber that may promote a feeling of fullness, potentially reducing calorie intake
5-HTP (5-Hydroxytryptophan)	5-HTP (5-Hydroxytryptophan): 5-HTP is a compound that the body produces from tryptophan. It's a precursor to serotonin, a neurotransmitter that may influence appetite and mood
African Mango (Irvingia gabonensis)	Some studies propose that African mango extract may have weight loss benefits by reducing body fat and improving metabolic parameters
Capsaicin	Capsaicin may increase thermogenesis, leading to an increase in calorie expenditure. It may also have appetite-suppressing effects. Found in chili peppers, capsaicin may help boost metabolism and reduce appetite. It's often included in some weight loss supplements
Apple Cider Vinegar	The acetic acid in apple cider vinegar may influence metabolism, reduce insulin resistance, and improve satiety. Although more research is needed, some studies suggest that apple cider vinegar may help reduce body weight and fat by promoting a feeling of fullness and enhancing metabolism.

Table 4: Some nutraceuticals that have significant role in obesity reduction

Discussion

Obesity is associated with a myriad of metabolic consequences that affect various organ systems in the body. Understanding these consequences is crucial for developing effective strategies for obesity management. Obesity is a major risk factor for insulin resistance, where cells become less responsive to insulin. This can lead to elevated blood glucose levels, eventually contributing to the development of type 2 diabetes [63]. Insulin resistance is a central feature of metabolic syndrome and plays a key role in the pathogenesis of diabetes. Obesity often leads to an abnormal lipid profile characterized by elevated levels of triglycerides, LDL cholesterol, and decreased levels of HDL cholesterol. Dyslipidemia is a significant cardiovascular risk factor, contributing to atherosclerosis and heart disease [64]. Adipose tissue in obese individuals can produce inflammatory molecules. Chronic low-grade inflammation is associated with obesity and contributes to various metabolic disorders. Inflammation is implicated in insulin resistance, cardiovascular diseases, and other obesity-related complications. Excess fat accumulation in the liver, known as hepatic steatosis, is common in obesity and can progress to non-alcoholic fatty liver disease. NAFLD can lead to liver inflammation, fibrosis, and, in severe cases, cirrhosis. It is closely linked to insulin resistance. Obesity contributes to the development of atherosclerosis, hypertension, and other cardiovascular risk factors. Increased risk of heart attacks, strokes, and other cardiovascular events in obese individuals. Adipose tissue acts as an endocrine organ, secreting hormones and adipokines [65]. Obesity can disrupt hormonal balance, affecting appetite regulation and metabolism. Hormonal imbalances may contribute to further weight gain, creating a feedback loop that exacerbates obesity. Obesity is a major risk factor for obstructive sleep apnea, where excess fat around the neck and throat can lead to intermittent airflow blockages during sleep. Sleep apnea can result in disrupted sleep patterns, daytime fatigue, and is associated with cardiovascular problems. Excess body weight puts increased stress on joints, particularly in the knees and hips [66]. Obesity is a significant risk factor for osteoarthritis and other musculoskeletal disorders. Addressing the metabolic consequences of obesity requires a comprehensive approach, including lifestyle modifications, dietary interventions, regular physical activity, and, in some cases, pharmacological or surgical interventions [67]. Early intervention and sustained efforts towards weight management are crucial for mitigating the long-term health risks associated with obesity. A multidisciplinary approach involving healthcare professionals such as nutritionists, endocrinologists, and physical therapists is often necessary for effective management [68]. The use of nutra-

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